CTR GRANT # 847

PROGRESS REPORT NO. 1

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Dates covered:

July 1, 1972 - July 1, 1973

3',5' Cyclic Monophosphate System in Carcinogenesis

Summary of Findings to Date:

The cyclic AMP system of the following cells is under investigation:

Fischer Rat Embryo - normal fibroblast, F111

Fischer Rat Embryo - 3-MC transformed, F2412

Fischer Rat Embryo - RLV transformed, F1849

Fischer Rat Embryo - High passage, non-transformed, F1706

Lakeview Syrian Hamster - transformed by fraction 9 from cigarette tars

Lakeview Syrian Hamster - normal control

Adenylate cyclase of the cells was measured (basal and fluoride stimulated) throughout the growth cycle. The basal level of the carcinogen transformed cells rises when the cells reach confluency, whereas the normal control cells continue to decrease. Treatment of the cells with trypsin, standard procedure to remove the cells from the petri dish surface, causes a considerable increase in the adenylate cyclase of the normal cell, but little or no change in the carcinogen-treated cells. This effect of trypsin suggests an alteration in the membrane of the carcinogen-treated cell has occurred.

The cyclic AMP pool of the cells was measured throughout the growth cycle. As might be expected from the elevated adenylate

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Source: https://www.industrydocuments.ucsf.edu/docs/pzyl0000

cyclase, the cyclic AMP level of all the cells is increased at 0 and 8 hours, and then starts decreasing. This decrease continues throughout the growth cycle, and the lowest levels are found at confluency. This is definitely not an expected result in view of previous data obtained by us and others.

Cyclic AMP inhibition curves were established for each of the cell lines. A very marked difference in the response of the normal and carcinogen-treated cells to cyclic AMP was observed. The normal cells are inhibited as much as 90% in cell division by cyclic AMP, whereas the carcinogen-treated cells are unaffected by cyclic AMP. Further investigation suggests this is due to the decreased ability of the tumor cells to transport cyclic AMP. This is particularly interesting because the inability to transport cyclic AMP may be the loss of an important control mechanism. Much of the control of cell division in an organ or tissue may result from the transcellular transport of cyclic AMP. A cell unable to transport cyclic AMP would lose the inhibiting and differentiating effects of cyclic AMP that is common to all the normal cells in the tissue.

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Source: https://www.industrydocuments.ucsf.edu/docs/pgyl0000